Medline

The human EBNA-2 coactivator p100: multidomain organization and relationship to the staphylococcal nuclease fold and to the tudor protein involved in Drosophila melanogaster development.

Callebaut I, Mornon JP

Biochem J 1997 Jan 321 (Pt 1):125-32

BROWSE : Biochem J • Volume 321 (Pt 1)

VIEW : **MEDLINE**, full MEDLINE, related records

Abstract

The human p100 protein was recently identified as a coactivator of the Epstein-Barr virus nuclear antigen 2. On the basis of sequence analysis with the hydrophobic cluster analysis method, we predict that this protein consists of a repeat of four similar domains. Their fold can be related to the staphylococcal nuclease structure whose first subdomain belongs to the large oligonucleotide/oligosaccharide-binding (OB)-fold superfamily. The catalytic amino acids present in nucleases are missing, however, suggesting that these repeated motifs could only serve to bind DNA without catalytic activity, as in many other OB-folds. A highly modified fifth domain follows the four nuclease-like domains, conserving the second subdomain of the nuclease structure but not the first one (the OB-fold), which is replaced by an original domain found in multiple copies in the tudor protein, a Drosophila melanogaster protein required during oogenesis for establishment of a functional posterior organizing centre. We named this heretofore undescribed domain the 'tudor domain' and highlight within it five invariant residues which could be involved in one of the essential roles played by these proteins.

MeSH

Amino Acid Sequence; Animal; Drosophila melanogaster; Epstein-Barr Virus Nuclear Antigens; Human; Insect Hormones; Micrococcal Nuclease; Models, Molecular; Molecular Sequence Data; Nuclear Proteins; Sequence Alignment; Support, Non-U.S. Gov't

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Solution structure of the active domain of tissue inhibitor of metalloproteinases-2. A new member of the OB fold protein family.

Williamson RA, Martorell G, Carr MD, Murphy G, Docherty AJ, Freedman RB, Feeney J
Biochemistry 1994 Oct 33:11745-59

BROWSE : Biochemistry • Volume 33 • Issue 39
VIEW : **MEDLINE**, full MEDLINE, related records

Abstract

Homonuclear two-dimensional and three-dimensional 1H nuclear magnetic resonance spectroscopy has been used to obtain essentially complete sequence-specific assignments for 123 of the 127 amino acid residues present in the truncated form of tissue inhibitor of metalloproteinases-2 (delta TIMP-2), the active N-terminal domain of the protein. Analysis of the through-space nuclear Overhauser effect data obtained for delta TIMP-2 allowed determination of both the secondary structure of the domain and also a low-resolution tertiary structure defining the protein backbone topology. The protein contains a five-stranded antiparallel beta-sheet that is rolled over on itself to form a closed beta-barrel, and two short helices which pack close to one another on the same barrel face. A comparison of the delta TIMP-2 structure with other known protein folds reveals that the beta-barrel topology is homologous to that seen in proteins of the oligosaccharide/oligonucleotide binding (OB) fold family. The common structural features include the number of beta-strands and their arrangement, the beta-barrel shear number, an interstrand hydrogen bond network, the packing of the hydrophobic core, and a conserved beta-bulge. Superpositions of the beta-barrels from delta TIMP-2 and two previously known members of the OB protein fold family (staphylococcal nuclease and Escherichia coli heat-labile enterotoxin) confirmed the similarity in beta-barrel topology. The three-dimensional structure of delta TIMP-2 has allowed a more detailed interpretation than was previously possible of the functional significance of available protein sequence and site-directed mutagenesis data for the TIMP family. Furthermore, the structure has revealed conserved surface regions of potential functional importance.

MeSH

Amino Acid Sequence; Binding Sites; Comparative Study; Magnetic Resonance Spectroscopy; Metalloendopeptidases; Models, Molecular; Molecular Sequence Data; Peptide Fragments; Protein Conformation; Protein Structure, Secondary; Proteins; Recombinant Proteins; Sequence Homology, Amino Acid; Solutions; Support, Non-U.S. Gov't; Tissue Inhibitor-of Metalloproteinase-2

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Medline

Structure of the single-stranded-DNA-binding domain of replication protein A bound to DNA.

Bochkarev A, Pfuetzner RA, Edwards AM, Frappier L

Nature 1997 Jan 385:176-81

BROWSE : Nature • Volume 385 • Issue 6612

VIEW : **MEDLINE**, full MEDLINE, related records

Abstract

The single-stranded-DNA-binding proteins (SSBs) are essential for DNA function in prokaryotic and eukaryotic cells, mitochondria, phages and viruses. The structures of four SSBs have been solved, but the molecular details of the interaction of SSBs with DNA remain speculative. We report here the crystal structure at 2.4 A resolution of the single-stranded-DNA-binding domain of human replication protein A (RPA) bound to DNA. Replication protein A is a heterotrimeric SSB that is highly conserved in eukaryotes. The largest subunit, RPA70, binds to single-stranded (ss) DNA and mediates interactions with many cellular and viral proteins. The DNA-binding domain, which lies in the middle of RPA70, comprises two structurally homologous subdomains oriented in tandem. The ssDNA lies in a channel that extends from one subdomain to the other. The structure of each RPA70 subdomain is similar to those of the bacteriophage SSBs, indicating that the mechanism of ssDNA-binding is conserved.

MeSH

Amino Acid Sequence; Cloning, Molecular; Crystallography, X-Ray; DNA; DNA-Binding Proteins; Escherichia coli; Human; Models, Molecular; Molecular Sequence Data; Protein Binding; Protein Conformation; Recombinant Proteins; Support, Non-U.S. Gov't

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